Kourous A. Rezaei, MD
Chair, International Affairs Committee

Global Trends in Retina Survey Compares Medical Retina Treatment Choices Worldwide

The ASRS International Affairs Committee thanks the members of the 36 retina societies around the world who participated in the second Global Trends in Retina Survey, conducted in conjunction with the 17th Annual ASRS Preferences and Trends (PAT) Survey.

Africa/Middle East

ARAB AFRICAN SOCIETY of Retina Specialists
IRANIAN VITREORETINA SOCIETY
ISRAEL OPHTHALMOLOGY SOCIETY
The Jordanian Ophthalmological Society
LEBANESE OPHTHALMOLOGICAL SOCIETY
VRSN
OMAN OPHTHALMIC SOCIETY
SAUDI OPHTHALMOLOGICAL SOCIETY

Asia/Pacific

ANZSRS Australian and New Zealand Society of Retinal Specialists
CHINESE OCULAR FUNDUS SOCIETY
PERDAMI
JRVS
SINGAPORE SOCIETY OF OPHTHALMOLOGY
RETINA SRI LANKA
ASSOCIATION OF VITREO-RETINA SPECIALISTS OF SRI LANKA
TRS TAIWAN Retina Society
Vitreo-Retinal Society of India
THE THAI RETINA SOCIETY

Europe

AUSTRIAN OPHTHALMOLOGICAL SOCIETY
BEAVRS
BRITISH AND EIRE ASSOCIATION OF VITREORETINAL SURGEONS
VRTL dutch society VITREORETINAL surgery
EURETINA
EUROPEAN SOCIETY OF RETINA SPECIALISTS
European VitreoRetinal Society
Club Francophone des Spécialistes de la Rétine
CFSR
FRENCH SOCIETY OF RETINA SPECIALISTS
GVRS
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Latin America

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BRAZILIAN RETINA AND VITREOUS SOCIETY
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COLOMBIAN RETINA AND VITREOUS ASSOCIATION
AOCR Asociación Oftalmológica de Costa Rica
COSTA RICAN ASSOCIATION OF OPHTHALMOLOGY
ASOCIACION MEXICANA DE RETINA, A.C.
MEXICAN RETINA ASSOCIATION
Sociedad Panamericana de Retina y Vítreo
PAN-AMERICAN RETINA AND VITREOUS SOCIETY
PERUVIAN SOCIETY OF OPHTHALMOLOGY
ASVR Asociación Salvadoreña de Vítreo y Retina
SALVADORAN RETINA AND VITREOUS ASSOCIATION
asuo Asociación Uruguaya de Oftalmólogos
URUGUAYAN ASSOCIATION OF OPHTHALMOLOGY

PART 2: MEDICAL RETINA HIGHLIGHTS

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The 2015 Global Trends in Retina Survey gathered a total of 1059 responses—making it the widest-reaching retina survey ever conducted.

The fall *Retina Times* (available at www.asrs.org/retina-times) featured part 1 of the medical retina result highlights. Here, we present part 2 of the survey's medical retina highlights and compare the international responses with the answers of 587 US ASRS members who responded to the same 15 clinical questions in the 2015 PAT Survey.

To view the complete 2015 Global Trends in Retina Survey results online, visit http://www.asrs.org/international/global-trends-in-retina.

Survey responses are grouped into 5 regions for ease of analysis. We thank our thought leaders for participating in the following roundtable discussion of this year's survey.

How would you treat a recent central retinal vein occlusion (CRVO) with vision-affecting macular edema?

Ahmad M. Mansour—Africa/Middle East: There is a 3-year lag period between US Food and Drug Administration (FDA) approval of Eylea (aflibercept, Regeneron Pharmaceuticals, Inc, Tarrytown, NY) and its use in the Middle East. The low use of Eylea reflects the slow regulatory process in implementation of new drugs in the Middle East. Plus, Eylea is currently the most expensive anti-VEGF drug and is perceived by many health agencies or insurers as a second-line therapy to be used when failure occurs with other anti-VEGF agents.

Taiji Sakamoto—Asia/Pacific: These results have something to do with the health insurance system of each country. In Japan, Avastin (bevacizumab, Genentech, Inc, South San Francisco, CA) is not used as frequently as it used to be because Lucentis (ranibizumab, Genentech, Inc) and Eylea are approved by the national health insurance. In some Asian countries, the health insurance system is not well organized or well funded; therefore, patients have to pay and are more sensitive to the price—ie, Lucentis and Eylea may be too expensive for them.

Use of Eylea is growing rapidly because it is effective. Further, Eylea is cheaper than Lucentis in Japan. Patients with CRVO are generally younger than those with AMD. Therefore, we do not have to be concerned as much for the systemic adverse events. On the other hand, Avastin use is off-label and we are moving away from it because of liability issues.

Maddalena Quaranta-El Maftouhi—Europe: In some European countries, Avastin has been approved for treatment of retinal diseases. In France, however, until now we have had only 2 therapeutic options: Lucentis and Ozurdex (dexamethasone intravitreal implant, Allergan, Inc, Irvine, CA). Regarding Eylea, the authorization of use and its reimbursement by social insurance have been very recently obtained, so it is not surprising that it is not commonly used.

Lihteh Wu—Latin America: The choice of pharmacologic treatment for macular edema secondary to CRVO will greatly depend on who pays for the treatment (ie, government vs private insurance vs self pay). In places where there are more self-paying patients, Avastin is king.

Eylea is a relative newcomer as an approved therapy for macular edema secondary to CRVO. I suspect that in the 2016 survey, Eylea will gain momentum at the expense of Lucentis. The use of Ozurdex is somewhat surprising and may have to do with its longer half-life compared with other agents. Ozurdex is not available yet in many Latin American countries.

Marco Zarbin—United States: I view the frequency of aflibercept (19.7%) and ranibizumab (16.3%) use for CRVO as equivalent. That fact is not surprising because both agents have been shown to be effective in randomized, multicenter, controlled clinical trials. As the results of these studies are well known and as there seems to be no material difference in efficacy between the 2 agents, I would not expect there to be a difference in the frequency of their use.

What is your initial treatment choice for a 72-year-old patient with branch retinal vein occlusion (BRVO), macular edema, and visual acuity of 20/60 (decreased vision)?

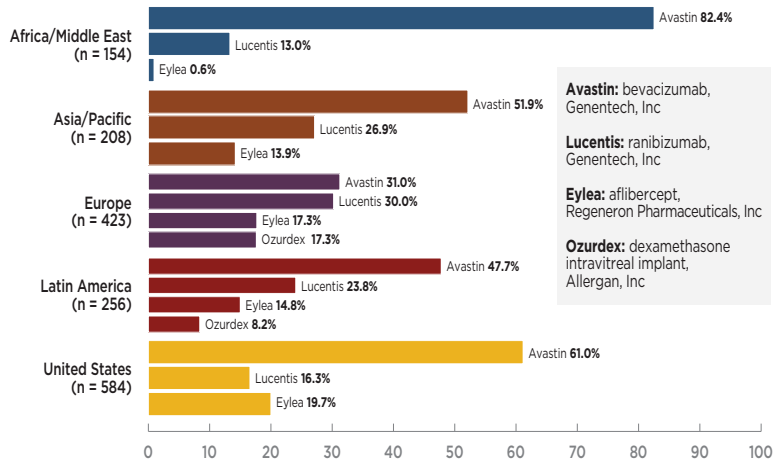
Ahmad M. Mansour—Africa/Middle East: Avastin is still the most popular drug in Africa and the Middle East due to its low cost and the large percentage of the population not having insurance coverage.

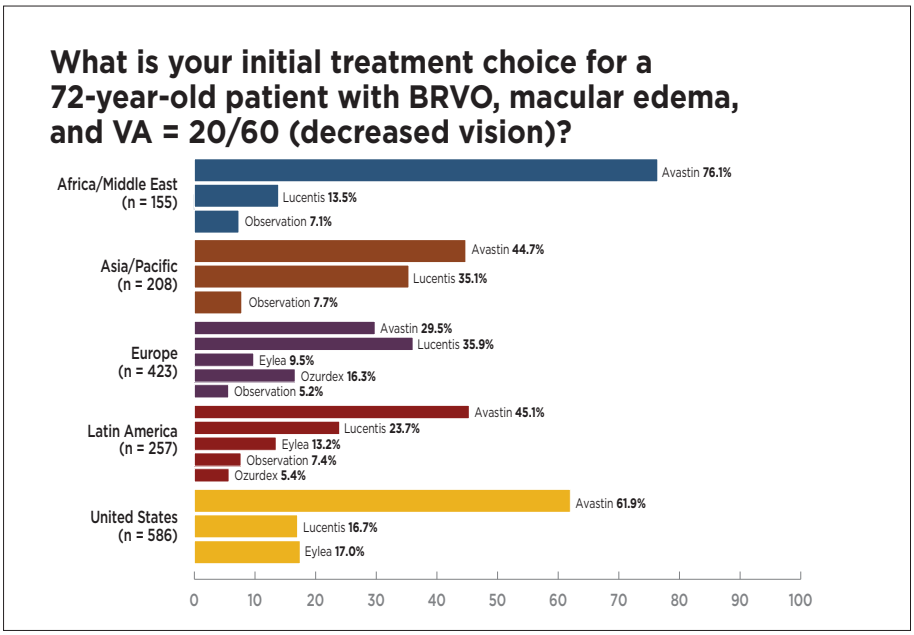
Taiji Sakamoto—Asia/Pacific: As stated above, the present key factor in treatment choice in Asia/Pacific is the price, not the drug's effectiveness or safety profile.

Maddalena Quaranta-El Maftouhi—Europe: Both Lucentis and Ozurdex can be used (and are refunded by social insurance) as first-line treatment for macular edema secondary to BRVO. Patients need fewer injections per year with Ozurdex and 30% of them need only 1 injection. For chronic macular edema, Ozurdex and Lucentis are normally used. The choice between the 2 drugs takes into account the patient's compliance and the risk of cataract from repeated Ozurdex injections. In France as well as many other European countries, Avastin and Eylea are not approved for this indication.

Lihteh Wu—Latin America: In Latin America, most retinal vein occlusions are managed the same way whether they are BRVO, hemiretinal vein occlusion, (HRVO), or CRVO. The choice of pharmacologic treatment will greatly depend on who pays for the treatment—the government, private insurance, or the patient.

How would you treat a recent CRVO with vision-affecting macular edema?





Marco Zarbin—United States: Unlike the 4 international groups, the US respondents did not choose "observation" as one of their top treatment options. Data from randomized, controlled clinical trials indicate that delaying treatment by more than 6 months results in a worse visual outcome for DME, as shown in the RIDE/RISE studies[1] and RVO (including CRVO) as indicated in the CRUISE study, and BRVO as shown in the BRAVO study.[2] Some experts estimate a 10% loss in final BCVA for every month that treatment is delayed. I suspect these results motivate US specialists to offer treatment earlier rather than later for patients with BRVO.

After how many injections do you consider an alternative anti-VEGF therapy for diabetic macular edema (DME) in a nonresponder?

Ahmad M. Mansour—Africa/Middle East: Middle Eastern patients are very impatient and would change their physician (doctor shopping) if they did not get a quick clinical response—hence, the push for a shift in anti-VEGF agents early on in most clinics in the Middle East.

Taiji Sakamoto—Asia/Pacific: Historically, in Asia/Pacific, we have had more treatment options for DME than for AMD. For example, vitrectomy has been preferred in Japan more than in the United States for treating DME. Subthreshold laser treatment may also be effective and may be the third-line therapy.

Because of the availability of multiple lines of therapy, we tend to switch more quickly from one drug to another for treating DME than for treating AMD. From my point of view, this may be more a psychological reaction rather than a logical approach.

Maddalena Quaranta-El Maftouhi—Europe: The number of injections prior to switching in France is normally lower, and the majority of retina specialists tend to switch after the loading phase. This was probably due to a lack of consensus concerning the term of "nonresponder," and the literature hasn't helped to solve this issue until now.

First, the clinical trials propose intensive treatment protocols, at least during the first 6 months, while retina specialists tend to reduce the number of visits and injections. Second, diabetic patients outside the clinical trials are generally less compliant than those participating in clinical trials.

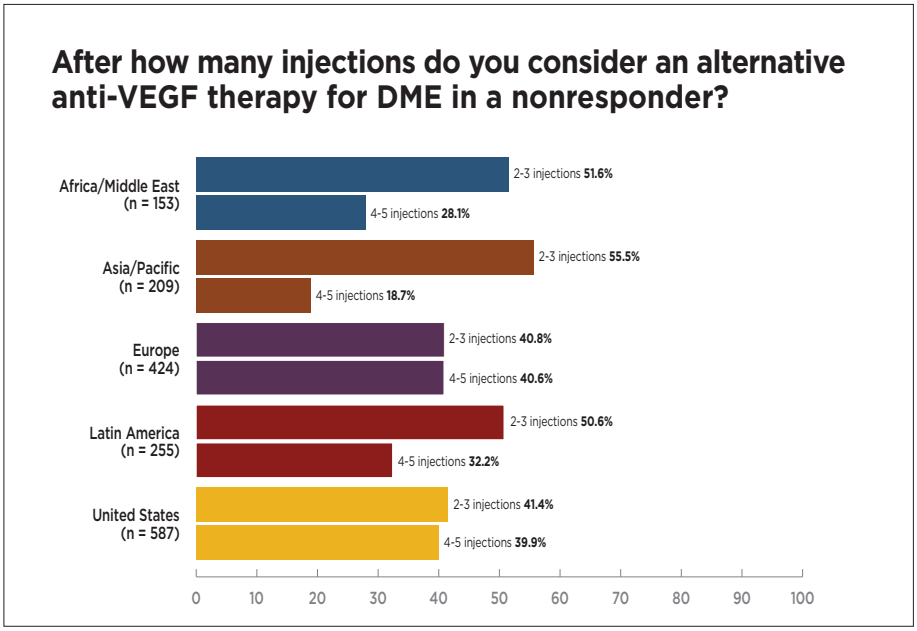
To switch in these cases means to try to obtain more rapid anatomic and functionally significant results as well as to increase patients' compliance.

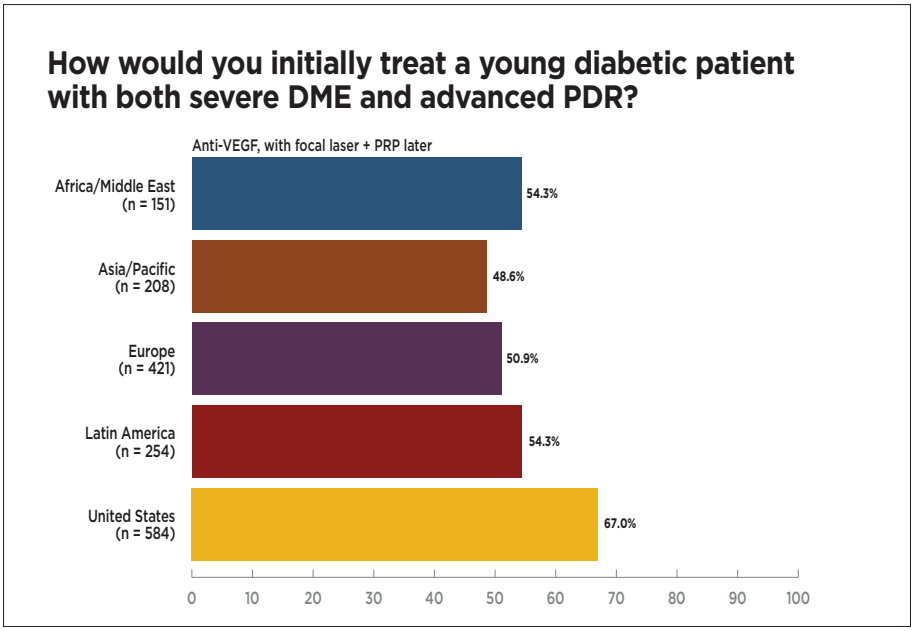
Lihteh Wu—Latin America: Most physicians in Latin America do not make a distinction between AMD vs RVO vs DME when choosing an anti-VEGF agent and treatment pattern. They consider the patient's response after 2 to 3 injections as enough evidence to make a decision as to whether an eye is nonresponsive and to switch the treatment.

Marco Zarbin—United States: The data indicate that US and European ophthalmologists are prone to give more injections before switching to an alternative anti-VEGF agent than ophthalmologists in other regions. Perhaps US and European ophthalmologists are influenced by the results of the DRCR.net Protocol I[3] and the RESTORE trials,[4] both of which indicate that the average number of injections required during the first year of therapy is 7 to 9 for 0.5 mg ranibizumab.

The structure of the VIVID/VISTA trials required 5 monthly injections of aflibercept 2 mg followed by injections every 8 weeks for the 2 mg cohort, which gives approximately 8 injections during the first year of therapy.[5] Of course, the number of injections required decreases dramatically by year 3, according to the results of the Protocol I and RESTORE trials.

Thus, one might expect to give approximately 8 anti-VEGF injections during the first year of therapy, which is close to the 9 to 10 injections required to control DME in year 1 of the Protocol T trial.





How would you initially treat a young diabetic patient with both severe DME and advanced proliferative diabetic retinopathy (PDR)?

Ahmad M. Mansour—Africa/Middle East: Nearly 55% of retina specialists in Africa and the Middle East choose anti-VEGF, with focal laser followed by panretinal photocoagulation (PRP) because the patient wants a quick response; intravitreal injection leads to improvement of vision by decreasing the edema while PRP would take care of ischemia. Also, there is a popular conception among ophthalmologists and patients that PRP alone may lead to increased macular edema and lower vision.

Taiji Sakamoto—Asia/Pacific: Before the anti-VEGF era, we had only laser treatment. Obviously, laser treatment induces collateral damage to the retina. Currently the treatment of choice is simultaneous anti-VEGF treatment and PRP. Research studies are currently evaluating the potential for anti-VEGF treatment in proliferative diabetic retinopathy and may be the future answer.

Maddalena Quaranta-El Maftouhi—Europe: Despite the fact that anti-VEGF therapy associated with focal laser initially, followed by PRP is the preferred answer of respondents, there is no evidence that this is the most effective solution. Focal laser in association with anti-VEGF treatment actually gives slightly worst functional results than anti-VEGF therapy alone.

Sustained and properly conducted anti-VEGF therapy seems to have long-term beneficial effects on the severity of PDR, avoiding the side effects of laser photocoagulation to the peripheral retina.

The survey respondents' answers vary slightly from one region to another. These differences probably depend on the habit of performing laser photocoagulation, the cost and access to chronic anti-VEGF treatment, and the compliance of the patient.

The DRCR.net results concerning focal laser and PRP (DRCR.net Protocol I and Protocol S)[3,6] will potentially relegate focal and peripheral laser photocoagulation to the role of rescue therapy. We will continue, however, to perform PRP in noncompliant patients or in the most complicated cases to consolidate the results and/or reduce the number of injections.

Lihteh Wu—Latin America: Most regions outside the US show a similar response to this case. It appears that most practitioners believe that anti-VEGF treatment would impact the vascular permeability and neovascular component simultaneously.

Marco Zarbin—United States: I suspect that the majority of US respondents prefer anti-VEGF therapy initially followed by focal laser and PRP later because the anti-VEGF therapy will address both the neovascularization and the retinal edema. Subsequently, PRP can be added to consolidate treatment of the neovascularization, and additional anti-VEGF injections can be used to treat retinal edema with focal laser added as rescue therapy for the edema if needed.

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Financial Disclosures

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